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Award Number: W81XWH-10-1-0786

TITLE: Regenerative Medicine and Restoration of Joint Function

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CONTRACTING ORGANIZATION: McMaster University
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REPORT DATE: February 2014

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland
21702-5012

DISTRIBUTION STATEMENT: Approved for Public
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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE February 2014		2. REPORT TYPE Final		3. DATES COVERED 27Sep2010 - 26Sep2013	
4. TITLE AND SUBTITLE Regenerative Medicine and Restoration of Joint Function				5a. CONTRACT NUMBER W81XWH-10-1-0786	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Dr. Paul Zalzal Associates: Ehsan Toyserkani; Hurtig Marc; Grynpas Michael; Mark McKee Marilyn Boitano; Robert Pilliar; Rita Kandel E-Mail: paulzalzal@gmail.com				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) McMaster University Hamilton, Ontario				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT Currently amputation, arthrodesis (joint fusion), or joint replacement are used to treat a joint with an intra-articular fracture or destroyed by a combat injury. Generation of personalized, anatomically shaped biological implants formed using techniques of regenerative medicine in conjunction with biodegradable biomaterial structures to restore a damaged articular joint surface to normal tissue structure, form and function is one way to overcome the limitations associated with current treatment methods. The aims of this study are to: 1) identify the parameters that generate anatomically shaped bone substitutes of optimal composition and structure with an articulating profile. 2) to develop a source of chondrocytes that can generate sufficient amounts of a cartilage layer to cover the bone substitute; and 3) to evaluate the structures formed in a preclinical model. The ongoing studies will further our understanding of the regulation of cell differentiation to chondrocytes and the bone substitute properties required to form a biological joint replacement.					
15. SUBJECT TERMS None Listed					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	5	19b. TELEPHONE NUMBER (include area code)

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INTRODUCTION

The complexity of extremity injuries as a consequence of battlefield trauma requires multifaceted reconstructions and has resulted in the need to develop entirely new treatment options to achieve limb salvage and thus full rehabilitation. **The overall aim of this research project was to develop large anatomically shaped biological implants formed using techniques of regenerative medicine in conjunction with biodegradable biomaterial structures to restore a damaged articular joint surface to normal tissue structure, form and function. The surgical methods to evaluate these implants in a pre-clinical sheep model was developed.** Our multi-disciplinary team was focused on generating medial tibial plateau and a large segment of the medial femoral condyle (knee joint) biphasic implants (definitive care of battle injuries). The approach we developed has resulted in an implant that can be customized contoured to replace the portion of the knee joint disrupted either by an intra-articular fracture or trauma. Being able to generate personalized implants is a critical feature given that most combat injuries are irregularly shaped.

Using an approach that allows for the formation of living tissues for joint reconstruction offers the advantage of functional tissue integration as well as adaptation to loading conditions during use which should avoid implant failure that can result from the fatigue or wear of synthetic biomaterial. This approach allows the generation of an implant of any contour, making this approach particularly appropriate for individuals who have irregular-shaped defects as a result of a combat injury. Three issues had to be overcome before these large biphasic constructs can be

used clinically, particularly in the military setting, are 1) the identification of an accessible human cell source to generate a large quantity of cartilage tissue; 2) the methodology to easily, rapidly and reliably generate custom-made CPP bone substitutes of desired shape; 3) develop a pre-clinical animal model to evaluate these implants. This report will summarize the results obtained during this grant period.

As my portion of the project is intertwined and interdependent with all aspects of this research, my final report would be identical to Dr. Rita Kandel (Toronto, Ontario, Canada). For this reason we have submitted only one final report. Please refer to her report for information.

KEYWORDS:

Joint restoration, cartilage tissue engineering, bone substitute biomaterial, cartilage repair